REMARKS

A. State of the Claims

Claims 1, 4-11, and 63-70 were pending prior to the Office Action dated February 13, 2004. Claims 1, 4, 5, and 63 have been amended herein. Claims 4 and 5 were amended simply to correct a clerical error in antecedent basis. Support for the amendment to claims 1 and 63 can be found in the specification at least on page 58. Claim 64 is cancelled. Claim 71 has been added. Support for this amendment can be found at pages 20 (3rd paragraph) and 58. Therefore, claims 1, 4-11, 63, and 65-71 are the subject of this response.

B. Claims Are Definite

The Action rejects the claims under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "infectious." It alleges that the specification "indicates that the sequence be capable of yielding an infectious GBV-C particle from an infected cell." It also states that neither the specification nor the declaration by Jack Stapleton, M.D., have defined the structures that distinguish the instantly claimed nucleic acid molecule as "infectious" over the prior art molecules. It further notes that a comparison of SEQ ID NO:1 and a sequence in one of the cited art references (Kim) "indicates that the sequence differences are located throughout the entire 9395 nt sequences" and that "the feature that makes the instant molecule infectious cannot be correlated with a specific structure." It concludes, "It remains unclear how Applicant's nucleic acid sequence yields and [sic] infectious clone while the prior art references using a similar experimental procedure set out in the instant specification does not." Applicants respectfully traverse this rejection.

"The primary purpose of this requirement if definiteness of claim language is to ensure that the scope of the claim is clear so the public is informed of the boundaries of what constitutes infringement of the patent." MPEP § 2173, at 2100-163 (7th ed.). In this case, the claims generally recite, "An isolated and purified DNA encoding an infectious GBV-C, wherein the DNA comprises a nucleic acid sequence encoding an amino acid sequence that is at least 99% identical to SEQ ID NO:2." The public knows that the claims cover a DNA molecule that includes a nucleic acid sequence encoding an amino acid sequence that is at least 99% identical to SEQ ID NO:2 and that is infectious—in other words, "capable of yielding an infectious GBV-C particle from an infected cell."

The arguments in the Action evidence this understanding because they show that the examiner appreciates the *functional* difference between the clone disclosed in the application and the clones disclosed in the prior art. As evidenced by the withdrawal of the art rejections in this case based on the Kim reference, the examiner understands and appreciates that the Kim reference's clone was not infectious, and thus, it was not "capable of yielding an infectious GBV-C particle from an infected cell." In contrast, the clone in the present case was infectious—that is, it was "capable of yielding an infectious GBV-C particle from an infected cell." There is no question regarding what the term "infectious" means, which is the relevant inquiry with respect to whether the claim is definite or indefinite regarding this term. The Action's arguments concerning the structure of an infectious clone are not applicable to whether the claim is definite. That the Action raises questions regarding the *structural* differences between the clones that renders one "infectious" and the other "not infectious" does not mean that the term "infectious" is indefinite. Instead, the relationship between structure and function is an issue that may be

more appropriately addressed by the other §112 requirements for patentability (which the examiner has also raised and Applicants address *supra*).

The term "infectious" is not unclear to the skilled person in the art. Consequently, this rejection should be withdrawn.

C. Claims Are Enabled

The Action rejects claims 1-4, 6-11, and 63-70 as lacking enablement. It contends that the specification does not teach any "particular structure for the claimed 'infectious' DNA." It again asserts the reference of Pang *et al.* ("Pang"), saying that the goal of the authors need not be to produce an infectious flavivirus. It states that Pang "clearly shows that a virus construct from the same family of viruses will allow for the replication of the heterologous nucleic acid but they do not produce particles and are thereby not infectious." Action at page 4. The Action contends that Pang "clearly indicates that more is required in order to produce an infectious nucleic acid." *Id.* Applicants respectfully traverse this rejection.

As argued earlier by Applicants, it is one thing to have never had an infectious clone and another thing to have an infectious clone and be able to make variants of it. In the present case, the Pang reference shows merely that noninfectious clones were available. At the time, no one had ever made an infectious GVB-C clone, and it was not the goal of the Pang authors to generate one in any event. Contrary to the statement in the Action, the goal of the Pang authors is relevant to any argument using this reference as evidence of nonenablement. The examiner is essentially contending that it provides an example of how would could have replicating DNA that was not infectious. However, if the goal of a set of experiments is *specifically not to produce* the claimed invention, how can that be evidence that a person of ordinary skill in the art cannot make the claimed invention? The Pang reference simply shows that if one wants to make

something that is nonfunctional as far as the claimed invention is concerned, he can accomplish that.

The Action ignores, however, the teaching of the present application, namely, the identification of an infectious clone. Once the skilled person has the teachings of the present invention—that is, the sequence of the infectious clone, the question is: would undue experimentation be required to make other infectious clones having a nucleic acid sequence encoding an amino acid sequence that is at least 99% identical to SEQ ID NO:2? In this case, it would not require undue experimentation because of the teachings of the specification and what was well known to those of skill of art at the time of the application. In addition to teaching the sequences of SEQ ID NO:1 (nucleic acid sequence) and SEQ ID NO:2 (polypeptide sequence encoded by portion of SEQ ID NO:1) of the infectious clone, the specification indicates:

- that the sequence of an RNA transcript can be manipulated, citing the references of Maniatis, 1989 and Ausubel, 1994, both of which are incorporated by reference (specification at page 20, first paragraph);
- that biologically equivalent polypeptides can be generated because of codon redundancy (specification at page 22, last paragraph), which is shown is Table 3 (page 59);
- that site-directed mutagenesis may be employed (specification at page 50, second paragraph);
- insertions, deletions, and substitutions in nucleic acid sequences can be identified using an RNAse cleavage assay and other assays (specification at page 56, paragraphs 2 and 5); and,
- substitutions and other changes can be made in a polypeptide, while preserving function (specification at pages 59-61)

The specification makes clear that a person of ordinary skill in the art could readily mutagenize the nucleic acid sequence of the infectious clone using techniques well known at the time of the invention or she could screen clinical isolates for alterations in nucleic acid sequence relative to SEQ ID NO:1. "The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available in the

public." MPEP 2164.05(a) (citing *inter alia*, *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q. 2d 1331, 1332 (Fed. Cir. 1991)). There is no contention to the contrary in the Action. Thus, the skilled artisan could take SEQ ID NO:1 and alter its sequence so that it contained a nucleic acid sequence encoding an amino acid sequence that is at least 99% identical to SEQ ID NO:2 and check whether such a sequence were infectious, according to the teachings of the specification. Moreover, that the claims recite a "a nucleic acid sequence encoding an amino acid sequence that is at least 99% identical to SEQ ID NO:2" means that a small and finite set of changes could be made in polyprotein and still be within the scope of the claims. And even though a skilled person would know about codon redundancy and how to make nucleic acid changes without affecting protein sequence at all or in a significant fashion, the specification provides a codon chart showing the redundancy and identifies conservative amino acid changes. *See* specification at least at Table 3 and pages 59-61. The implementation of such changes is routine experimentation.

The disclosure of an assay in the application for testing infectiousness indicates that a person of ordinary skill in the art could readily determine whether the functional limitation of the claim was met. Consequently, using well known recombinant DNA techniques and routine experimentation, the skilled artisan could make and use nucleic acids falling within the scope of the claimed invention without undue experimentation.

Alternatively, the skilled artisan could screen for endogenous GVB-C isolates based on alterations relative to SEQ ID NO:1. One could screen for such alterations using sequences from SEQ ID NO:1 in the assays described in the specification. The isolates could then be tested for infectiousness. This is another way other infectious GVB-C DNA with a nucleic acid sequence encoding an amino acid sequence that is at least 99% identical to SEQ ID NO:2 could be made.

Accordingly, the specification enables the full scope of the claimed invention.

D. Specification Describes Claimed Invention

The Action rejects claims 1, 4, 6-11, and 63-70 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. It contends that Applicants are claiming "a product based on function alone without providing sufficient description of the product." Action at page 8. It states, "Since the disclosure fails to describe common attributes or characteristics that identify members of the group, the disclosure of [a] single compound is insufficient to describe the genus of molecules encompassed by the claimed invention." Action at page 9. Applicants respectfully traverse this rejection.

There is no caselaw requiring that a correlation between structure and function be described in an application in order to fulfill the written description requirement. The MPEP specifically states, "For some biomolecules, examples of identifying characteristics include a **sequence**, structure, binding affinity, binding specificity, molecular weight, and length". MPEP §2163 (emphasis added). Moreover, reduction to practice of the claimed invention is not necessary to show possession of the invention.

Again, claim 1 states: "An isolated and purified DNA encoding an infectious GBV-C, wherein the DNA comprises a nucleic acid sequence encoding an amino acid sequence that is at least 99% identical to SEQ ID NO:2." The claim specifically recites that the DNA includes "a nucleic acid sequence encoding an amino acid sequence that is at least 99% identical to SEQ ID NO:2." The nucleic acid sequence encoding SEQ ID NO:2 is provided in the application, as well as a codon chart showing which codons encode which amino acids. Specification at page 59. Moreover, the specification identifies conservative amino acid changes. Pages 59-61. By reciting that the nucleic acid encodes certain amino acid sequences—those that are at least 99% identical

to SEQ ID NO:2—the claim is limited in scope to certain structures, in addition to being limited by function. The genus of molecules covered by the invention are described by common structural features. This is sufficient to describe adequately the claimed invention.

Claim 71 has been added and this claim does not recite that the DNA is "infectious." This claim is novel and nonobvious over the prior art and it does not have any functional limitations. Consequently, there should be no issue regarding tying structure to any function with this claim.

Furthermore, the dependent claims add further structural requirements. For example, claims 65-68 depend from claim 1 and recite that the "DNA comprises [500, 1000, 2000, or 5000] contiguous nucleotides that are identical or complementary to SEQ ID NO:1." The Action is incorrect to assert that the claims cover "structurally unrelated molecules" because any covered DNA has specific structural and functional features. The structural features are tied to SEQ ID NOs: 1 and 2, which are disclosed in the instant specification.

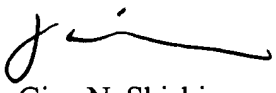
Thus, the claimed invention is properly described by the application. Accordingly, Applicants respectfully request that this rejection be withdrawn.

E. Conclusion

Applicants believe that the foregoing remarks fully respond to all outstanding matters for this application. Applicants respectfully request that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at (512) 536-3081 is respectfully requested.

Respectfully submitted,



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